

NMCP COVID-19 Literature Report #68: Friday, 21 May 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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The Big Picture

News in Brief

Emerging Zoonoses Like Coronaviruses

The WHO is convening a panel for the emergence and spread of zoonotic diseases ([WHO](#)).

Which is good, because... A novel coronavirus was isolated in hospitalized children with pneumonia in East Malaysia ([CIDRAP](#); see [Clin Infect Dis article for full report](#); insert "everything is fine dog.gif" here).

Dogs aren't the only animals that may be new/novel coronavirus sources – pigs are also implicated ([Science](#); see also: [medRxiv preprint](#)).

Not to be outdone, cats are getting in on this, too... An Italian serosurvey of pets suggests that cats appear to be more susceptible to SARS-CoV-2 infection than dogs ([Emerg Infect Dis](#)).

Public Health

Public health (and the CDC in particular) has a trust problem ([NPR](#)).

"CDC's slow, cautious messaging on Covid-19 seems out of step with the moment, public health experts say" ([STAT](#)).

Meanwhile, \$7.4 billion has been committed to hire more public health workers to boost the 'crumbling U.S. public health infrastructure' ([WP](#)).

Research Impacts

"How COVID is changing the study of human behaviour: The pandemic is teaching us key lessons about crisis, communication and misinformation, and is spurring changes in the way scientists study public-health questions" ([Nature](#)).

"A shortage of plastic pipette tips is delaying biology research: Extreme weather and the Covid-19 pandemic have upended supply chains for plastic lab equipment" ([Smithsonian](#)).

Long read: "How COVID broke the evidence pipeline: The pandemic stress-tested the way the world produces evidence — and revealed all the flaws" ([Nature](#); see also: [related editorial](#)).

Looking Ahead...

"How the Covid pandemic ends: Scientists look to the past to see the future" ([STAT](#)).

It's not going to come cheap though... the IMF says ending the pandemic may cost \$50 billion ([Reuters](#)).

Webinars

WHEN: Wednesday, 26 May 2021, 1700-1830 ET

WHAT: Learning to Live With COVID-19

Presented by the American Public Health Association (APHA) and National Academy of Medicine (NAM)

DETAILS: "The 19th COVID-19 Conversations webinar will discuss what the world will look like when COVID-19 is an endemic disease, what we can learn from seasonal influenza, the reality of managing future outbreaks, ethical considerations for future policymaking, and lessons current and future local policymakers can learn from the last year."

Participants can earn 1.5 CME.

REGISTER: <https://covid19conversations.org/Webinar-Registration>

FEMA, in coordination with the release of "COVID-19 Pandemic Operational Guidance: All-Hazards Incident Response and Recovery" (see Special Reports section below for more), is offering a series of webinars throughout the month of June to further educate people on the pandemic operational guidance. For more information, see:

<https://www.fema.gov/event/covid-19-pandemic-operational-guidance-webinars>

Webinar 1: Thursday, 03 June 2021 1000 ET | [Register for Webinar](#)

Webinar 2: Tuesday, 08 June 2021, 1500 ET | [Register for Webinar](#)

Webinar 3: Thursday, 10 June 2021, 1100 ET | [Register for Webinar](#)

Webinar 4: Wednesday, 16 June 2021, 1900 ET | [Register for Webinar](#)

Webinar 5: Thursday, 17 June 2021, 1300 ET | [Register for Webinar](#)

Special Reports and Other Resources

Independent Panel: [COVID-19: Make it the Last Pandemic](#) (May 2021)

For BLUF, short summary versions, see:

- "Covid pandemic should serve as 'Chernobyl moment' for global health reform, international experts say" ([STAT](#)).
- "How the world failed to curb COVID" ([Nature](#)).

"Since September 2020, the Independent Panel has systematically, rigorously and comprehensively examined why COVID-19 became a global health and socio-economic crisis.

In May 2021, the Independent Panel presented its findings and recommendations for action to curb the COVID-19 pandemic and to ensure that any future infectious disease outbreak does not become another catastrophic pandemic."

Website includes [summary \[pdf\]](#), [main report \[pdf\]](#), companion narrative, and 16 background documents.

"Transformational change recommended by the Independent Panel for Pandemic Preparedness and Response:

- Establish a high-level Global Health Threats Council led by heads of state and government. Adopt a political declaration by heads of state and government at a Special Session of the UN General Assembly committing to transforming pandemic preparedness and response. Adopt a Pandemic Framework Convention within the next 6 months.
- Establish the financial independence of WHO based on fully unearmarked resources and applying an increase in member states' fees to equate to two-thirds of the WHO base programme budget. Strengthen the authority and independence of the WHO Director-General, including by having a single term of office of 7 years with no option for re-election. The same rule should be adopted for WHO Regional Directors.
- Focus WHO's mandate on normative, policy, and technical guidance; empower WHO to take a leading, convening, and coordinating role in operational aspects of an emergency response to a pandemic, without, in most circumstances, taking on responsibility for procurement and supplies.
- All national governments to update their national preparedness plans against targets and benchmarks to be set by WHO within 6 months, ensuring that there are appropriate and relevant skills, logistics, and funding available to cope with future health crises.
- WHO to formalise universal periodic peer reviews as a means of accountability. The International Monetary Fund needs to include routinely a pandemic preparedness assessment, including an evaluation of economic policy response plans, as part of the Article IV consultation with member countries.
- WHO to establish a new global system for surveillance, based on full transparency by all parties, using digital tools.
- The World Health Assembly to give WHO both the explicit authority to publish information about outbreaks with pandemic potential immediately without requiring the prior approval of national governments and the ability to dispatch experts to investigate pathogens with pandemic potential with rapid and guaranteed right of access.

- Future declarations of a Public Health Emergency of International Concern should be based on the precautionary principle where warranted and on clear, objective, and published criteria.
- Transform the present ACT Accelerator into a truly global end-to-end platform to deliver the global public goods of vaccines, therapeutics, diagnostics, and essential supplies. Secure technology transfer and commitment to voluntary licensing in all agreements where public funding has been invested in research and development.
- Establish stronger regional capacities for manufacturing, regulation, and procurement of needed tools for equitable and effective access to vaccines, therapeutics, diagnostics, and essential supplies, as well as for clinical trials.
- Create an International Pandemic Financing Facility to mobilise long-term (10–15 year) contributions of approximately US\$5–10 billion per annum to finance preparedness. This facility should have the ability to disburse up to \$50–100 billion at short notice in the event of a crisis. Use existing global and regional organisations, based on their functions, to manage and channel the funds. There should be an ability-to-pay formula adopted whereby larger and wealthier economies will pay the most, preferably from non-overseas development assistance budget lines and additional to established overseas development assistance budget levels.
- The Global Health Threats Council will have the task of allocating and monitoring funding from this instrument to existing regional and global institutions, which can support development of pandemic preparedness and response capacities.
- Heads of state and government should appoint national pandemic coordinators who are accountable to them, and who have a mandate to drive whole-of-government coordination for pandemic preparedness and response." (from: [Lancet article](#))

FEMA: [COVID-19 Pandemic Operational Guidance All-Hazards Incident Response and Recovery \[pdf\]](#) (17 May 2021)

From [press release](#): "For more than a year, the emergency management community has been operating in a pandemic environment, and FEMA has emphasized the importance of all state, local, tribal and territorial (SLTT) governments applying lessons learned from 2020, as they prepare for operations in 2021. To aid in that effort, this document serves as a tool for governments, outlining not only guidance based on lessons learned and best practices, but also guidance related to new priorities that have arisen in recent months. This document builds upon the guidance released last year and:

- Describes continued challenges to disaster operations posed by COVID-19 and planning considerations, based on science and the best available data, for emergency managers in addressing those challenges.
- Outlines considerations for SLTT governments related to planning COVID-19 testing and vaccination operations. This includes an overview of how FEMA supports SLTTs to

establish and operate testing facilities and vaccination sites that ensure fair and equitable distribution of vaccines to all individuals who want one.

- Provides updated resources (e.g., checklists, reports, and other guidance) reflecting current lessons learned and best practices for operating in a pandemic environment to enable emergency managers to best adapt response and recovery plans.
- Outlines how FEMA plans to continue adapting response and recovery operations to the evolving COVID-19 risks to ensure prioritization for life safety, life sustainment, workforce protection and to maintain the delivery of FEMA's programs."

NAM: [National Organizations Share Strategies to Improve Crisis Standards of Care Implementation During Future COVID-19 Surges and Beyond](#) (13 May 2021)

"The prospect of once again facing decisions about whether to transition to crisis standards of care (CSC) calls for action now, while a relative lull in cases allows stakeholders to plan thoughtfully for such decisions. This is especially important in light of painful lessons the pandemic has taught about the need for clarity and consistency across institutions and jurisdictions about invoking CSC and the disproportionate impact COVID-19 has had on historically minoritized and marginalized populations. Going forward, addressing equity must be recognized as a vital consideration for refining and deploying CSC. The challenge of CSC that are not sensitive to issues of equity can be compounded when they are put into practice through processes that similarly fail to embed considerations of equity."

Includes additional resources such as links to guidelines from signatory associations.

CSIS: [What Has Covid-19 Taught Us about Strengthening the DOD's Global Health Security Capacities?](#) (11 May 2021)

"The Covid-19 pandemic has led to millions of deaths and cases of enduring illness, destabilized economies, diminished U.S. international standing, and exposed the U.S. military to challenges not experienced in over a century. Since the pandemic began, the U.S. Department of Defense (DOD) has been heavily involved in addressing challenges to the armed forces while supporting the overall national Covid-19 response.

Future biological threats will undoubtedly present new challenges. Yet broad U.S. military expertise in health, biosecurity, and biosafety will continue to contribute substantially to coordinated, interagency global health security efforts. [This report includes] five recommendations for how the Biden-Harris administration and members of Congress can help steer impending deliberations over the future of the DOD's contributions to global health security. As U.S. diplomatic engagement expands to address the worsening vaccine crisis and other related global health security challenges, there will soon be increased calls for the DOD to contribute in new and important ways that draw on its exceptional logistics, planning, lift, and scientific capacities. These recommendations are meant to complement the excellent and extensive [recent analysis by Mark Cancian and Adam Saxton](#) of the CSIS

International Security Program on how the U.S. military responded to Covid-19 to guarantee the protection and readiness of U.S. forces and how it supported the civilian pandemic response at home. That study and this white paper are both part of the work of the CSIS Commission on Strengthening America's Health Security.

Broad U.S. military expertise in health, biosecurity, and biosafety will continue to contribute substantially to coordinated, interagency global health security efforts."

Modern War Institute: [Toward A Whole-Of-Society Framework For Countering Disinformation](#) (10 May 2021)

This article is part of a series: [Full-Spectrum: Capabilities and Authorities in Cyber and the Information Environment](#)

"Disinformation is the deliberate dissemination of false or erroneous information in order to discredit a person, organization, product, or notion. Disinformation is used as a tactic by actors ranging from Russia's campaign to weaken democratic and international institutions to terrorist groups' recruitment efforts to the growing anti-vaccine movement. JD Maddox, Casi Gentzel, and Adela Levis describe a framework for countering disinformation that would entail not only "counter messaging but also of proactive measures that use facts to inform audiences, reduce the impact of disinformation, and promote freedom of expression." The framework categorizes efforts as communication, resilience, disruption, or regulation. Proactive communication before disinformation (or misinformation) can gain a foothold is critical and requires "implementation of the full spectrum of communication capabilities." Further, increasing transparency and building trust in democratic values and institutions are needed. Building resilience to disinformation will include activities such as improving digital literacy; promoting independent, fact-based, investigative journalism; and leveraging public diplomacy. Disruption leverages technology to prevent the spread of disinformation through various tools and techniques such as blocking or cyberspace operations. Regulation – including legislation and international cooperation - should seek input from local and national legislators, media associations, internet platforms and the broader tech sector, and international organizations." (summary from [Pandora Report 5.14.2021](#))

Peer-Reviewed Articles

Nat Med: [Health systems resilience in managing the COVID-19 pandemic: lessons from 28 countries](#) (17 May 2021)

"Health systems resilience is key to learning lessons from country responses to crises such as coronavirus disease 2019 (COVID-19). In this perspective, we review COVID-19 responses in 28 countries using a new health systems resilience framework. Through a combination of

literature review, national government submissions and interviews with experts, we conducted a comparative analysis of national responses. We report on domains addressing governance and financing, health workforce, medical products and technologies, public health functions, health service delivery and community engagement to prevent and mitigate the spread of COVID-19. We then synthesize four salient elements that underlie highly effective national responses and offer recommendations toward strengthening health systems resilience globally."

MMWR: [Modeling of Future COVID-19 Cases, Hospitalizations, and Deaths, by Vaccination Rates and Nonpharmaceutical Intervention Scenarios — United States, April–September 2021](#)
(14 May 2021)

"What is already known about this topic? Increases in COVID-19 cases in March and early April occurred despite a large-scale vaccination program. Increases coincided with the spread of SARS-CoV-2 variants and relaxation of nonpharmaceutical interventions (NPIs).

What is added by this report? Data from six models indicate that with high vaccination coverage and moderate NPI adherence, hospitalizations and deaths will likely remain low nationally, with a sharp decline in cases projected by July 2021. Lower NPI adherence could lead to substantial increases in severe COVID-19 outcomes, even with improved vaccination coverage.

What are the implications for public health practice? High vaccination coverage and compliance with NPIs are essential to control COVID-19 and prevent surges in hospitalizations and deaths in the coming months."

NEJM: [The Covid-19 Infodemic — Applying the Epidemiologic Model to Counter Misinformation](#)
(12 May 2021)

"We believe the intertwining spreads of the virus and of misinformation and disinformation require an approach to counteracting deceptions and misconceptions that parallels epidemiologic models by focusing on three elements: real-time surveillance, accurate diagnosis, and rapid response....

Social determinants of health and individual behaviors contribute to community-level variation in infectious disease risk. Similarly, people's information environment, psychology (e.g., uncertainty avoidance), and information-consumption habits contribute to their susceptibility to questionable content. As a result, the likelihood of acceptance of disinformation and misinformation varies. Our model will be more effective for people intrigued by misinformation but not yet under its thrall than for committed acolytes sequestered in echo chambers."

SARS-CoV-2 Variants

News in Brief

"WHO names B1617 fourth COVID-19 variant of concern" ([CIDRAP](#)).

"Vaccines seem to work well against coronavirus variants. It's also complicated" ([STAT](#)).

"How a worrisome coronavirus variant spread unnoticed: A new variant stealthily took hold on two continents, highlighting the need for global genomic surveillance" ([Nature](#)).

Podcast: "The variant blamed for India's catastrophic second wave" ([Nature](#)).

Webinars

WHAT: COVID-19 Conversations: Variants and Vaccines

Presented by the American Public Health Association (APHA) and National Academy of Medicine (NAM)

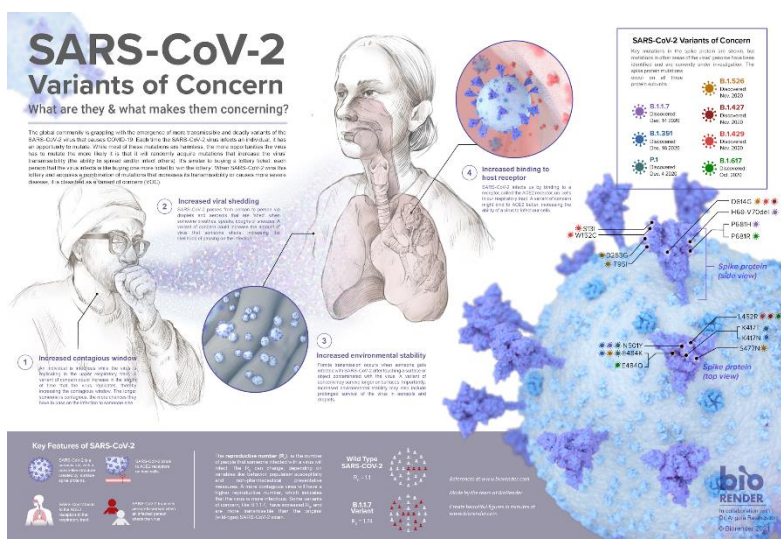
DETAILS: "The 18th COVID-19 Conversations webinar focused on emerging COVID-19 variants, how vaccines can adapt to these new variants, and other interventions that could help curb transmission."

WEBSITE: <https://covid19conversations.org/Webinars/variants> – includes links to presenter slides, transcript, and recording [YouTube]

Special Reports and Other Resources

Bio Render: [Infographic on SARS-CoV-2 Variants of Concern](#) (13 May 2021)

Dr. Angela Rasmussen, a virologist and research scientist with the Georgetown Center for Global Health Science and Security and VIDO-InterVac at the University of Saskatchewan, developed an infographic explaining the most important features of the newest SARS-CoV-2 variants.



Peer-Reviewed Articles

PNAS: [Just 2% of SARS-CoV-2-positive individuals carry 90% of the virus circulating in communities](#) (10 May 2021)

"We analyze data from the fall 2020 pandemic response efforts at the University of Colorado Boulder, where more than 72,500 saliva samples were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using qRT-PCR. All samples were collected from individuals who reported no symptoms associated with COVID-19 on the day of collection. From these, 1,405 positive cases were identified. The distribution of viral loads within these asymptomatic individuals was indistinguishable from what has been previously observed in symptomatic individuals. Regardless of symptomatic status, ~50% of individuals who test positive for SARS-CoV-2 seem to be in noninfectious phases of the disease, based on having low viral loads in a range from which live virus has rarely been isolated. We find that, at any given time, just 2% of individuals carry 90% of the virions circulating within communities, serving as viral 'supercarriers' and possibly also superspreaders."

Vaccines and Vaccine Hesitancy

News in Brief

Novavax is unlikely to seek an EUA for its experimental coronavirus vaccine in the US until July ([WP](#)).

"Mix-and-match COVID vaccines trigger potent immune response: Preliminary results from a trial of more than 600 people are the first to show the benefits of combining different vaccines" ([Nature](#)).

Delaying the second shot may boost immune response, especially in older adults ([Nature](#); see also: [medRxiv preprint](#)).

Supply and Demand

The FDA says that undiluted, thawed vials of the Pfizer covid vaccine can be stored for up to one month at refrigerator temperatures ([FDA](#)).

Need an incentive to get the COVID-19 vaccine? You can get a free ride to a vaccination site from Uber or Lyft ([CNN](#)), a pound of free crawfish ([Nola](#)), or possibly (a lot) cash, depending on where you live ([Fox News](#); [NPR](#)).

Messaging and Mis/Disinformation Sources

"Just 12 people are behind most vaccine hoaxes on social media, research shows" ([NPR](#); see also: [Center for Countering Digital Hate report #1 \[pdf\]](#) and [CCDH report #2 \[pdf\]](#)).

HHS has released a user guide and toolkit of resources to help build vaccine confidence in rural communities ([HHS](#)). They also produce other kits to target other groups as part of the COVID-19 public education campaign; see: <https://wecandothis.hhs.gov/resources>.

Hesitancy and Antivax

"How truth decay is fueling vaccine hesitancy" ([RAND](#)).

Long read: "They haven't gotten a covid vaccine yet. But they aren't 'hesitant' either. Much has been said about people opposed to or skeptical of coronavirus vaccines. But there's another group that has yet to get shots, and their reasons are more complex" ([NYT](#)).

Webinars

ICYMI: The [recording \(registration required to view\)](#) and [slides \[pdf\]](#) from ASPR TRACIE's webinar "Be a COVID-19 Vaccine Champion" are now available.

Peer-Reviewed Articles

JAMA Otolaryngol Head Neck Surg: [Preliminary Analysis of Association Between COVID-19 Vaccination and Sudden Hearing Loss Using US Centers for Disease Control and Prevention Vaccine Adverse Events Reporting System Data](#) (20 May 2021)

"This cross-sectional study examines the national incidence of sudden sensorineural hearing loss after COVID-19 vaccination using data from the CDC Vaccine Adverse Events Reporting System....

These preliminary findings of VAERS data in the early phase of societal COVID-19 vaccination using 2 messenger RNA vaccines suggest that no association exists between inoculation with a SARS-CoV-2 messenger RNA vaccine and incident sudden hearing loss. While the reporting period did not include other vaccines that are currently in use, we hope these findings will reassure health care clinicians and patients to receive all scheduled doses of the vaccination as recommended by current public health guidelines."

Clin Infect Dis: [The effectiveness of the TWO-DOSE BNT162b2 vaccine: analysis of real-world data](#) (17 May 2020)

"COVID-19 mRNA vaccines were shown to be highly efficacious in preventing the disease in randomized controlled trials; nonetheless, evidence on the real-world effectiveness of this vaccine is limited. Study objective was to evaluate the effectiveness of BNT162b2 [Pfizer] vaccine in preventing SARS-CoV-2 infection and COVID-19-related hospitalization and mortality.

This historical cohort study included members of a large health provider in Israel that were vaccinated with at least one dose of BNT162b2. The primary outcome was incidence rate of a SARS-CoV-2 infection confirmed with rt-PCR, between 7 to 27 days after second dose (protection-period), as compared to days 1 to 7 after the first dose, where no protection by the vaccine is assumed (reference-period).

Data of 1,178,597 individuals vaccinated with BNT162b2 were analyzed (mean age 47.7 years [SD=18.1], 48.4% males) of whom 872,454 (74.0%) reached the protection period. Overall, 4514 infections occurred during the reference period compared to 728 during the protection period, yielding a weighted mean daily incidence of 54.8 per 100,000 (95%CI: 26.1-115.0 per 100,000) and 5.4 per 100,000 (95%CI: 3.5-8.4 per 100,000), respectively. The vaccine effectiveness in preventing infection was 90% (95%CI:79%- 95%) and 94% (95%CI:88%-97%) against COVID-19. Among immunosuppressed patients, vaccine effectiveness against infection was 71% (95%CI:37%-87%). The adjusted hazard ratios for hospitalization in those infected were 0.82 (95%CI:0.36-1.88), 0.45 (95%CI:0.23-0.90), and 0.56 (95%CI:0.36-0.89) in the age groups 16-44, 45-64 and 75 and above, respectively.

The effectiveness of the BNT162b2 vaccine is comparable to the one reported in the phase III clinical trial."

Clin Infect Dis: [Immediate reactions following the first dose of the SARS-CoV2 mRNA vaccines do not preclude second dose administration](#) (14 May 2021)

"Addressing COVID19 vaccine hesitancy and minimizing potential vaccine contraindications are critical to combat the ongoing pandemic. We describe a practical approach to immediate adverse events after the first dose of the SARS-CoV2 mRNA vaccines, focusing on allergic reactions with respect to their diagnosis and management."

MMWR: [Interim Estimates of Vaccine Effectiveness of Pfizer-BioNTech and Moderna COVID-19 Vaccines Among Health Care Personnel — 33 U.S. Sites, January–March 2021](#) (14 May 2021)

"What is already known about this topic? Health care personnel (HCP) are at high risk for COVID-19. The early distribution of two mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna) to HCP provided an opportunity to examine vaccine effectiveness in a real-world setting.

What is added by this report? The first U.S. multisite test-negative design vaccine effectiveness study among HCP found a single dose of Pfizer-BioNTech or Moderna COVID-19 vaccines to be 82% effective against symptomatic COVID-19 and 2 doses to be 94% effective.

What are the implications for public health practice? The mRNA vaccines are highly effective at preventing symptomatic COVID-19 among U.S. HCP. High vaccination coverage among HCP and the general population is critical to prevent COVID-19 in the United States."

MMWR: [Demographic and Social Factors Associated with COVID-19 Vaccination Initiation Among Adults Aged ≥65 Years — United States, December 14, 2020–April 10, 2021](#) (14 May 2021)

"What is already known about this topic? Older adults have experienced higher risk for COVID-19–associated morbidity and mortality and therefore have been prioritized for COVID-19 vaccination.

What is added by this report? After the first 3.5 months of the U.S. COVID-19 vaccination program, 79.1% of adults aged ≥65 years had received ≥1 dose, with higher vaccination initiation among men. Counties with lower vaccination initiation rates had higher percentages of older adults with social vulnerabilities.

What are the implications for public health practice? Monitoring demographic and social factors affecting COVID-19 vaccine access for older adults and prioritizing efforts to ensure equitable access to COVID-19 vaccine are needed to ensure high coverage among this group."

JAMA Dermatol: [Delayed Localized Hypersensitivity Reactions to the Moderna COVID-19 Vaccine: A Case Series](#) (12 May 2021)

"Question What are the clinical course and histopathologic examination findings for delayed injection-site reactions to the Moderna coronavirus disease 2019 (COVID-19) vaccine?

Findings The Moderna COVID-19 vaccine may cause a delayed localized hypersensitivity reaction with a median latency to onset of 7 days after vaccine administration. This pruritic and variably tender reaction has a median duration of 5 days, but may persist for up to 21 days, and may occur again and sooner after the second vaccine dose; no serious adverse events were observed in association with this cutaneous reaction to the Moderna COVID-19 vaccine.

Meaning Self-limited localized delayed hypersensitivity reactions to the Moderna COVID-19 vaccine may occur, and in contrast with immediate hypersensitivity reactions, these delayed hypersensitivity reactions are not a contraindication to subsequent vaccination."

Lancet: [Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data](#) (12 May 2021)

"> Research, from Com-COV study comparing mixed dosing schedules of Pfizer / Oxford-AstraZeneca vaccines, shows increase in the frequency of mild-moderate symptoms in those receiving either mixed dosing schedule

> Adverse reactions were short-lived, with no other safety concerns

> Impact of mixed schedules on immunogenicity unknown as yet, with data to follow from this study" (summary from [press release](#))

J Infect: [Impact of COVID-19 vaccination program on seroprevalence in blood donors in England, 2021](#) (10 May 2021)

"The COVID-19 vaccination programme commenced in England on 8th December 2020 primarily based on age; by 7th March 2021 approximately 93% of the English population aged 70+ years had received at least 1 dose of either the Pfizer BioNTech or AstraZeneca vaccines. Using a nucleoprotein assay that detects antibodies following natural infection only and a spike assay that detects infection and vaccine-induced responses, we aim to describe the impact of vaccination on SARS-CoV-2 antibody prevalence in English blood donors.

An estimated 93.5% of 70 to 84-year-old blood donors had antibodies against COVID-19 from late February 2021.

Only around 5% of 70 to 84-year old donors had antibodies from natural infection, which suggests the vaccine is producing a good immune response in older people following a single vaccine dose.

Prevalence of antibodies from natural infection have remained stable in older donors since late December 2020, suggestive of vaccine impact."

Nature: [Neutralizing antibody vaccine for pandemic and pre-emergent coronaviruses](#) (10 May 2021)

"Betacoronaviruses (betaCoVs) caused the severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) outbreaks, and the SARS-CoV-2 pandemic^{1–4}. Vaccines that elicit protective immunity against SARS-CoV-2 and betaCoVs circulating in animals have the potential to prevent future betaCoV pandemics. Here, we show that macaque immunization with a multimeric SARS-CoV-2 receptor binding domain (RBD) nanoparticle adjuvanted with 3M-052/Alum elicited cross-neutralizing antibody (cross-nAb) responses against batCoVs, SARS-CoV-1, SARS-CoV-2, and SARS-CoV-2 variants B.1.1.7, P.1, and B.1.351. Nanoparticle vaccination resulted in a SARS-CoV-2 reciprocal geometric mean neutralization ID₅₀ titer of 47,216, and protection against SARS-CoV-2 in macaque upper and lower respiratory tracts. Importantly, nucleoside-modified mRNA encoding a stabilized transmembrane spike or monomeric RBD also induced SARS-CoV-1 and batCoV cross-nAbs, albeit at lower titers. These results demonstrate current mRNA vaccines may provide some protection from future zoonotic betaCoV outbreaks, and provide a platform for further development of pan-betaCoV vaccines."

Treatments and Management

News in Brief

Did you know? The CDC has a Clinical Care Quick Reference for COVID-19 ([CDC](#)).

"WHO will test whether three existing drugs can save lives of hospitalized people" ([Nature](#)).

Peer-Reviewed Articles

Clin Infect Dis: [Differential Cytokine Signatures of SARS-CoV-2 and Influenza Infection Highlight Key Differences in Pathobiology](#) (20 May 2021)

"Several inflammatory cytokines are upregulated in severe COVID-19. We compared cytokines in COVID-19 versus influenza in order to define differentiating features of the inflammatory response to these pathogens and their association with severe disease. Because elevated body mass index (BMI) is a known risk factor for severe COVID-19, we examined the relationship of BMI to cytokines associated with severe disease.

Thirty-seven cytokines and chemokines were measured in plasma from 135 patients with COVID-19, 57 patients with influenza, and 30 healthy controls. Controlling for BMI, age, and sex, differences in cytokines between groups were determined by linear regression and random forest prediction was utilized to determine the cytokines most important in distinguishing severe COVID-19 and influenza. Mediation analysis was utilized to identify cytokines that mediate the effect of BMI and age on disease severity.

IL-18, IL-1 β , IL-6, and TNF- α were significantly increased in COVID-19 versus influenza patients while GM-CSF, IFN- γ , IFN- λ 1, IL-10, IL-15, and MCP-2 were significantly elevated in the influenza group. In subgroup analysis based on disease severity, IL-18, IL-6, and TNF- α were elevated in severe COVID-19, but not severe influenza. Random forest analysis identified high IL-6 and low IFN- λ 1 levels as the most distinct between severe COVID-19 and severe influenza. Finally, IL-1RA was identified as a potential mediator of the effects of BMI on COVID-19 severity.

These findings point to activation of fundamentally different innate immune pathways in SARS-CoV-2 and influenza infection, and emphasize drivers of severe COVID-19 to focus both mechanistic and therapeutic investigations."

Clin Infect Dis: [Factors Associated with Readmission in the US Following Hospitalization with COVID-19](#) (20 May 2021)

"Patients hospitalized for COVID-19 may experience complications following hospitalization and require readmission. This analysis estimates the rate and risk factors associated with COVID-19-related readmission and inpatient mortality.

This is a retrospective cohort study utilizing deidentified chargemaster data from 297 hospitals across 40 US states on patients hospitalized with COVID-19 February 15-June 09, 2020. Demographics, comorbidities, acute conditions, and clinical characteristics of first hospitalization are summarized. Multivariable logistic regression was used to measure risk factor associations with 30-day readmission and in-hospital mortality.

Among 29,659 patients, 1,070 (3.6%) were readmitted. Readmitted patients were more likely to have diabetes, hypertension, cardiovascular disease (CVD), chronic kidney disease (CKD) vs those not readmitted ($p < 0.0001$) and to present on first admission with acute kidney injury (15.6% vs. 9.2%), congestive heart failure (6.4% vs. 2.4%), and cardiomyopathy (2.1% vs. 0.8%) ($p < 0.0001$). Higher odds of readmission were observed in patients age > 60 vs. 1840 (odds ratio [OR]=1.92, 95% confidence interval [CI]=1.48, 2.50), and admitted in the Northeast vs. West (OR=1.43, 95% CI=1.14, 1.79) or South (OR=1.28, 95% CI=1.11, 1.49). Comorbidities including diabetes (OR=1.34, 95% CI=1.12, 1.60), CVD (OR=1.46, 95% CI=1.23, 1.72), CKD stage 1-5 (OR=1.51, 95% CI=1.25, 1.81) and stage 5 (OR=2.27, 95% CI=1.81, 2.86) were associated with higher odds of readmission. 12.3% of readmitted patients died during second hospitalization.

Among this large US population of patients hospitalized with COVID-19, readmission was associated with certain comorbidities and acute conditions during first hospitalization. These findings may inform strategies to mitigate risks of readmission due to COVID-19 complications."

JAMA Netw Open: [Characteristics Associated With Multisystem Inflammatory Syndrome Among Adults With SARS-CoV-2 Infection](#) (19 May 2021)

"This cohort study uses data from the Vizient Clinical Data Base to examine hospital discharge rates and outcomes of hospitalizations as well as demographic factors among US patients with ischemic stroke before and during the COVID-19 pandemic."

See also: [invited commentary](#)

Open Forum Infect Dis: [Impact of bamlanivimab monoclonal antibody treatment on hospitalization and mortality among non-hospitalized adults with SARS-CoV-2 infection](#) (17 May 2021)

"Monoclonal antibody treatment may prevent complications of COVID-19. We sought to quantify the impact of bamlanivimab monoclonal antibody monotherapy on hospitalization and mortality among outpatients at high risk of COVID-19 complications.

In this observational study we compared outpatients who received bamlanivimab monoclonal antibody from December 9, 2020 to March 3, 2021 to non-treated patients with a positive polymerase chain reaction or antigen test for SARS-CoV-2 during the same period who were eligible for monoclonal antibody treatment. The primary outcome was 28-day

hospitalization or all-cause mortality, and the secondary outcome was hospitalization or emergency department visit without hospitalization. The risk-adjusted odds of study outcomes comparing bamlanivimab treated and untreated patients was determined using 1:5 propensity matching and multivariable logistic regression.

Among 232 patients receiving bamlanivimab matched with 1,160 comparator patients, the mean age was 67 years, 56% were female, and 196 (14%) of patients experienced hospitalization or mortality. After adjustment for propensity to receive treatment, bamlanivimab treatment was associated with a significantly reduced risk-adjusted odds of hospitalization or mortality within 28 days (OR 0.40, 95% confidence interval [95% CI] 0.24 to 0.69; $p < .001$). Bamlanivimab treatment was also associated with a significantly lower risk adjusted odds of hospitalization or emergency department visit without hospitalization (OR 0.54, 95% CI 0.35 to 0.82; $p = .004$). The results were most strongly associated with patients age 65 years and older.

Bamlanivimab monoclonal antibody monotherapy was associated with reduced hospitalizations and mortality within 28 days among outpatients with mild-moderate COVID-19."

Clin Infect Dis: [Trends over time in the risk of adverse outcomes among patients with SARS-CoV-2 infection](#) (11 May 2021)

"We aimed to describe trends in adverse outcomes among patients who tested positive for SARS-CoV-2 between February and September 2020 within a national healthcare system.

We identified enrollees in the national U.S. Veterans Affairs healthcare system who tested positive for SARS-CoV-2 between 2/28/2020 and 9/30/2020 ($n = 55,952$), with follow-up extending to 11/19/2020. We determined trends over time in incidence of the following outcomes that occurred within 30 days of testing positive: hospitalization, intensive care unit (ICU) admission, mechanical ventilation and death.

Between February and July 2020, there were marked downward trends in the 30-day incidence of hospitalization (44.2% to 15.8%), ICU admission (20.3% to 5.3%), mechanical ventilation (12.7% to 2.2%), and death (12.5% to 4.4%), which subsequently plateaued between July and September 2020. These trends persisted after adjustment for sociodemographic characteristics, comorbid conditions, documented symptoms and laboratory tests, including among subgroups of patients hospitalized, admitted to the ICU or treated with mechanical ventilation. From February to September, there were decreases in the use of hydroxychloroquine (56.5% to 0%), azithromycin (48.3% to 16.6%) vasopressors (20.6% to 8.7%), and dialysis (11.6% to 3.8%) and increases in the use of dexamethasone (3.4% to 53.1%), other corticosteroids (4.9% to 29.0%) and remdesivir (1.7% to 45.4%) among hospitalized patients.

The risk of adverse outcomes in SARS-CoV-2-positive patients decreased markedly between February and July, with subsequent stabilization from July to September. These trends were not explained by changes in measured baseline patient characteristics and may reflect changing treatment practices or viral pathogenicity."

Lancet: [Convalescent plasma in patients admitted to hospital with COVID-19 \(RECOVERY\): a randomised controlled, open-label, platform trial](#) (14 May 2021)

"RECOVERY is the largest randomised trial to report results of the effect of convalescent plasma in patients hospitalised with COVID-19. We found that compared with usual care alone, high-titre convalescent plasma did not reduce 28-day mortality, the probability of discharge within 28 days, or the probability of progressing to the composite outcome of invasive mechanical ventilation or death in patients who were not receiving invasive mechanical ventilation at randomisation. We saw no evidence of any material benefit or hazard of convalescent plasma in any patient subgroup. Taking the results of all trials together, including RECOVERY which includes about eight-times as much information as all other trials combined, allocation to convalescent plasma was associated with a mortality rate ratio 0.98 (95% CI 0.91–1.06; $p=0.63$). For patients admitted to hospital with COVID-19, convalescent plasma offers no material therapeutic benefits."

Lancet Rheumatol: [Non-steroidal anti-inflammatory drug use and outcomes of COVID-19 in the ISARIC Clinical Characterisation Protocol UK cohort: a matched, prospective cohort study](#) (07 May 2021)

"Early in the pandemic it was suggested that pre-existing use of non-steroidal anti-inflammatory drugs (NSAIDs) could lead to increased disease severity in patients with COVID-19. NSAIDs are an important analgesic, particularly in those with rheumatological disease, and are widely available to the general public without prescription. Evidence from community studies, administrative data, and small studies of hospitalised patients suggest NSAIDs are not associated with poorer COVID-19 outcomes. We aimed to characterise the safety of NSAIDs and identify whether pre-existing NSAID use was associated with increased severity of COVID-19 disease.

This prospective, multicentre cohort study included patients of any age admitted to hospital with a confirmed or highly suspected SARS-CoV-2 infection leading to COVID-19 between Jan 17 and Aug 10, 2020. The primary outcome was in-hospital mortality, and secondary outcomes were disease severity at presentation, admission to critical care, receipt of invasive ventilation, receipt of non-invasive ventilation, use of supplementary oxygen, and acute kidney injury. NSAID use was required to be within the 2 weeks before hospital admission. We used logistic regression to estimate the effects of NSAIDs and adjust for confounding variables. We used propensity score matching to further estimate effects of NSAIDs while accounting for covariate differences in populations.

Between Jan 17 and Aug 10, 2020, we enrolled 78 674 patients across 255 health-care facilities in England, Scotland, and Wales. 72 179 patients had death outcomes available for matching; 40 406 (56·2%) of 71 915 were men, 31 509 (43·8%) were women. In this cohort, 4211 (5·8%) patients were recorded as taking systemic NSAIDs before admission to hospital. Following propensity score matching, balanced groups of NSAIDs users and NSAIDs non-users were obtained (4205 patients in each group). At hospital admission, we observed no significant differences in severity between exposure groups. After adjusting for explanatory variables, NSAID use was not associated with worse in-hospital mortality (matched OR 0·95, 95% CI 0·84–1·07; $p=0\cdot35$), critical care admission (1·01, 0·87–1·17; $p=0\cdot89$), requirement for invasive ventilation (0·96, 0·80–1·17; $p=0\cdot69$), requirement for non-invasive ventilation (1·12, 0·96–1·32; $p=0\cdot14$), requirement for oxygen (1·00, 0·89–1·12; $p=0\cdot97$), or occurrence of acute kidney injury (1·08, 0·92–1·26; $p=0\cdot33$).

NSAID use is not associated with higher mortality or increased severity of COVID-19. Policy makers should consider reviewing issued advice around NSAID prescribing and COVID-19 severity."

J Pharm Pract: [Treatment of Severe Hypertriglyceridemia With Insulin Infusions in Severe COVID-19: A Case Series](#) (22 April 2021)

"Rapid onset of severe hypertriglyceridemia was quickly recognized in critical COVID-19 patients. Associated causes have been due to secondary hemophagocytic lymphohistiocytosis (HLH) syndrome, medication-induced, or acute liver failure. Statins, omega-3 polyunsaturated acids, niacin, and fibrates are common oral lipid lowering therapy options in patients at risk for hypertriglyceridemia. The severity of hypertriglyceridemia in COVID-19 patients with triglyceride values reaching greater than 1,000 mg/dL put them at a heightened risk of pancreatitis and therefore an essential need to acutely lower their levels. We present a case series of 5 patients who achieved rapid triglyceride lowering through continuous insulin infusion therapy.

A retrospective chart review of 48 critical COVID-19 patients who were admitted from March 22 to April 15, 2020 was conducted. Inclusion criteria consisted of mechanical ventilation and continuous insulin infusion to treat severe hypertriglyceridemia resulting with 5 eligible patients in this case report.

In addition to standard oral lipid lowering therapies, continuous insulin infusion successfully treated severe hypertriglyceridemia in critically ill COVID-19 patients. None of the patients experienced pancreatitis or hypoglycemia necessitating cessation of insulin. Further studies are needed to show the optimum dose and duration of insulin infusion as monotherapy and in combination with oral therapies."

Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases

Peer-Reviewed Articles

JAMA Netw Open: [Assessment of the Association of Vitamin D Level With SARS-CoV-2 Seropositivity Among Working-Age Adults](#) (19 May 2021)

"Question Are low levels of vitamin D independently associated with the risk of SARS-CoV-2 seropositivity?

Findings In this cohort study of 18 148 individuals whose vitamin D levels were measured before the COVID-19 pandemic, low levels of vitamin D were associated with SARS-CoV-2 seropositivity in unadjusted univariable analysis. However, after adjusting for potentially confounding factors, including age, sex, race/ethnicity, education, body mass index, blood pressure, smoking status, and geographical location, vitamin D level was not associated with SARS-CoV-2 seropositivity.

Meaning Although SARS-CoV-2–seropositive individuals did have lower vitamin D levels than seronegative individuals, low vitamin D levels were not independently associated with the risk of seropositivity."

See also: [invited commentary](#)

Nature: [Diverse Functional Autoantibodies in Patients with COVID-19](#) (19 May 2021)

"COVID-19 manifests with a wide spectrum of clinical phenotypes that are characterized by exaggerated and misdirected host immune responses. While pathological innate immune activation is well documented in severe disease¹, the impact of autoantibodies on disease progression is less defined. Here, we used a high-throughput autoantibody (AAb) discovery technique called Rapid Extracellular Antigen Profiling (REAP) to screen a cohort of 194 SARS-CoV-2 infected COVID-19 patients and healthcare workers for autoantibodies against 2,770 extracellular and secreted proteins (the "exoproteome"). We found that COVID-19 patients exhibit dramatic increases in autoantibody reactivities compared to uninfected controls, with a high prevalence of autoantibodies against immunomodulatory proteins including cytokines, chemokines, complement components, and cell surface proteins. We established that these autoantibodies perturb immune function and impair virological control by inhibiting immunoreceptor signaling and by altering peripheral immune cell composition, and found that murine surrogates of these autoantibodies exacerbate disease severity in a mouse model of SARS-CoV-2 infection. Analysis of autoantibodies against tissue-associated antigens revealed associations with specific clinical characteristics and disease severity. In summary, these findings implicate a pathological role for exoproteome-directed autoantibodies in COVID-19 with diverse impacts on immune functionality and associations with clinical outcomes."

JAMA Netw Open: [Characteristics and Outcomes Among US Patients Hospitalized for Ischemic Stroke Before vs During the COVID-19 Pandemic](#) (17 May 2021)

"Question What were the hospital discharge rates, demographic factors, and outcomes of hospitalization associated with the COVID-19 pandemic among US patients with ischemic stroke (IS) in 2020?

Findings In this cohort study of 478 US hospitals with 324 013 patients with IS, substantial decreases in the number of patients discharged with IS were observed at the beginning of the pandemic in February 2020, but these rates returned to prepandemic levels by July 2020. Compared with patients with IS in 2019, those with IS and comorbid COVID-19 in 2020 were less likely to have conventional vascular risk factors or stroke at hospital admission and were more likely to be Black or Hispanic and to experience medical complications and in-hospital death.

Meaning Among patients with IS in 2020, comorbid COVID-19 was common, especially in Black and Hispanic populations, and in-hospital morbidity and mortality rates were high."

J Infect Dis: [Morbidity and Mortality among Adults Experiencing Homelessness Hospitalized with COVID-19](#) (16 May 2021)

"People experiencing homelessness (PEH) are at higher risk for chronic health conditions, but clinical characteristics and outcomes for PEH hospitalized with COVID-19 are not known. We analyzed population-based surveillance data of COVID-19-associated hospitalizations during March 1-May 31, 2020. Two percent of the people hospitalized with COVID-19 for whom a housing status was recorded were homeless. Of 199 cases in the analytic sample, most were of racial/ethnic minority groups, and had underlying health conditions. Clinical outcomes such as ICU admission, respiratory support including mechanical ventilation, and deaths were documented. Hispanic and Non-Hispanic Black persons accounted for most mechanical ventilation and deaths. Severe illness was common among persons experiencing homelessness who were hospitalized with COVID-19."

Hypertension: [First-Phase Ejection Fraction, a Measure of Preclinical Heart Failure, Is Strongly Associated With Increased Mortality in Patients With COVID-19](#) (10 May 2021)

"Presence of heart failure is associated with a poor prognosis in patients with coronavirus disease 2019 (COVID-19). The aim of the present study was to examine whether first-phase ejection fraction (EF1), the ejection fraction measured in early systole up to the time of peak aortic velocity, a sensitive measure of preclinical heart failure, is associated with survival in patients hospitalized with COVID-19. A retrospective outcome study was performed in patients hospitalized with COVID-19 who underwent echocardiography (n=380) at the West Branch of the Union Hospital, Wuhan, China and in patients admitted to King's Health Partners in South London, United Kingdom. Association of EF1 with survival

was performed using Cox proportional hazards regression. EF1 was compared in patients with COVID-19 and in historical controls with similar comorbidities (n=266) who had undergone echocardiography before the COVID-19 pandemic. In patients with COVID-19, EF1 was a strong predictor of survival in each patient group (Wuhan and London). In the combined group, EF1 was a stronger predictor of survival than other clinical, laboratory, and echocardiographic characteristics including age, comorbidities, and biochemical markers. A cutoff value of 25% for EF1 gave a hazard ratio of 5.23 ([95% CI, 2.85–9.60]; $P < 0.001$) unadjusted and 4.83 ([95% CI, 2.35–9.95], $P < 0.001$) when adjusted for demographics, comorbidities, hs-cTnI (high-sensitive cardiac troponin), and CRP (C-reactive protein). EF1 was similar in patients with and without COVID-19 (23.2 ± 7.3 versus $22.0 \pm 7.6\%$, $P = 0.092$, adjusted for prevalence of risk factors and comorbidities). Impaired EF1 is strongly associated with mortality in COVID-19 and probably reflects preexisting, preclinical heart failure."

Eur J Clin Microbiol Infect Dis: [Sex-specific impact of severe obesity in the outcomes of hospitalized patients with COVID-19: a large retrospective study from the Bronx, New York](#) (06 May 2021)

"It has been demonstrated that obesity is an independent risk factor for worse outcomes in patients with COVID-19. Our objectives were to investigate which classes of obesity are associated with higher in-hospital mortality and to assess the association between obesity and systemic inflammation. This was a retrospective study which included consecutive hospitalized patients with COVID-19 in a tertiary center. Three thousand five hundred thirty patients were included in this analysis (female sex: 1579, median age: 65 years). The median body mass index (BMI) was 28.8 kg/m². In the overall cohort, a J-shaped association between BMI and in-hospital mortality was depicted. In the subgroup of men, BMI 35–39.9 kg/m² and BMI ≥ 40 kg/m² were found to have significant association with higher in-hospital mortality, while only BMI ≥ 40 kg/m² was found significant in the subgroup of women. No significant association between BMI and IL-6 was noted. Obesity classes II and III in men and obesity class III in women were independently associated with higher in-hospital mortality in patients with COVID-19. The male population with severe obesity was the one that mainly drove this association. No significant association between BMI and IL-6 was noted."

JACC Cardiovasc Imaging: [Prospective Case-Control Study of Cardiovascular Abnormalities 6 Months Following Mild COVID-19 in Healthcare Workers](#) (05 May 2021)

"The purpose of this study was to detect cardiovascular changes after mild severe acute respiratory syndrome coronavirus 2 infection.

Concern exists that mild coronavirus disease 2019 may cause myocardial and vascular disease.

Participants were recruited from COVIDsortium, a 3-hospital prospective study of 731 health care workers who underwent first-wave weekly symptom, polymerase chain reaction, and serology assessment over 4 months, with seroconversion in 21.5% (n = 157). At 6 months post-infection, 74 seropositive and 75 age-, sex-, and ethnicity-matched seronegative control subjects were recruited for cardiovascular phenotyping (comprehensive phantom-calibrated cardiovascular magnetic resonance and blood biomarkers). Analysis was blinded, using objective artificial intelligence analytics where available.

A total of 149 subjects (mean age 37 years, range 18 to 63 years, 58% women) were recruited. Seropositive infections had been mild with case definition, noncase definition, and asymptomatic disease in 45 (61%), 18 (24%), and 11 (15%), respectively, with 1 person hospitalized (for 2 days). Between seropositive and seronegative groups, there were no differences in cardiac structure (left ventricular volumes, mass, atrial area), function (ejection fraction, global longitudinal shortening, aortic distensibility), tissue characterization (T1, T2, extracellular volume fraction mapping, late gadolinium enhancement) or biomarkers (troponin, N-terminal pro-B-type natriuretic peptide). With abnormal defined by the 75 seronegatives (2 SDs from mean, e.g., ejection fraction <54%, septal T1 >1,072 ms, septal T2 >52.4 ms), individuals had abnormalities including reduced ejection fraction (n = 2, minimum 50%), T1 elevation (n = 6), T2 elevation (n = 9), late gadolinium enhancement (n = 13, median 1%, max 5% of myocardium), biomarker elevation (borderline troponin elevation in 4; all N-terminal pro-B-type natriuretic peptide normal). These were distributed equally between seropositive and seronegative individuals.

Cardiovascular abnormalities are no more common in seropositive versus seronegative otherwise healthy, workforce representative individuals 6 months post-mild severe acute respiratory syndrome coronavirus 2 infection."

Asian Pac J Allergy Immunol: [Asthma does not increase COVID-19 mortality and poor outcomes: A systematic review and meta-analysis](#) (18 April 2021)

"The Center for Disease Control and Prevention (CDC) has mentioned Coronavirus Disease 2019 (COVID-19) patients with moderate or severe asthma as a high risk group for severe illness. While WHO mentioned only chronic respiratory diseases, not specifically asthma as a risk factor for severe illness. There has been asthma prevalence discrepancy in studies of COVID-19 across the world.

This meta-analysis aims to investigate the association between asthma and composite poor outcome in patients with coronavirus disease (COVID-19).

We conducted a systematic literature search from PubMed and Embase database. We included all original research articles with adult COVID-19 patients > 18 years old and had information related to asthma as a risk factor. Studies with outcomes consisting of

mortality, severe COVID-19, use of mechanical ventilation, ICU admission, and hospital admission were included in this study. The outcomes of interest were divided into severe COVID-19, mortality and other poor outcomes.

Eleven studies were included in meta-analysis with a total of 6,046 patients. Asthma was not associated with composite poor outcomes with OR = 0.92 (95%CI 0.71-1.19, $p = 0.61$, and $I^2 = 8.49\%$). Furthermore, subgroup analysis showed that asthma was not associated with severe COVID ($p = 0.76$), mortality ($p = 0.45$), and other poor outcomes ($p = 0.28$).

Our study showed that asthma was not associated with severe COVID-19, mortality, and other poor outcomes in patients with COVID-19."

Long COVID / Post-COVID Period

News in Brief

"Researchers fear people of color may be disproportionately affected by long Covid" ([STAT](#)).

Peer-Reviewed Articles

BMJ: [Risk of clinical sequelae after the acute phase of SARS-CoV-2 infection: retrospective cohort study](#) (19 May 2021)

"Objective To evaluate the excess risk and relative hazards for developing incident clinical sequelae after the acute phase of SARS-CoV-2 infection in adults aged 18-65.

Design Retrospective cohort study.

Setting Three merged data sources from a large United States health plan: a large national administrative claims database, an outpatient laboratory testing database, and an inpatient hospital admissions database.

Participants Individuals aged 18-65 with continuous enrollment in the health plan from January 2019 to the date of a diagnosis of SARS-CoV-2 infection. Three comparator groups, matched by propensity score, to individuals infected with SARS-CoV-2: a 2020 comparator group, an historical 2019 comparator group, and an historical comparator group with viral lower respiratory tract illness.

Main outcome measures More than 50 clinical sequelae after the acute phase of SARS-CoV-2 infection (defined as the date of first SARS-CoV-2 diagnosis (index date) plus 21 days) were identified using ICD-10 (international classification of diseases, 10th revision) codes. Excess risk in the four months after acute infection and hazard ratios with Bonferroni corrected 95% confidence intervals were calculated.

Results 14% of adults aged ≤ 65 who were infected with SARS-CoV-2 (27 074 of 193 113) had at least one new type of clinical sequelae that required medical care after the acute phase of the illness, which was 4.95% higher than in the 2020 comparator group. The risk for specific new sequelae attributable to SARS-Cov-2 infection after the acute phase, including chronic respiratory failure, cardiac arrhythmia, hypercoagulability, encephalopathy, peripheral neuropathy, amnesia (memory difficulty), diabetes, liver test abnormalities, myocarditis, anxiety, and fatigue, was significantly greater than in the three comparator groups (2020, 2019, and viral lower respiratory tract illness groups) (all $P < 0.001$). Significant risk differences because of SARS-CoV-2 infection ranged from 0.02 to 2.26 per 100 people (all $P < 0.001$), and hazard ratios ranged from 1.24 to 25.65 compared with the 2020 comparator group.

Conclusions The results indicate the excess risk of developing new clinical sequelae after the acute phase of SARS-CoV-2 infection, including specific types of sequelae less commonly seen in other viral illnesses. Although individuals who were older, had pre-existing conditions, and were admitted to hospital because of covid-19 were at greatest excess risk, younger adults (aged ≤ 50), those with no pre-existing conditions, or those not admitted to hospital for covid-19 also had an increased risk of developing new clinical sequelae. The greater risk for incident sequelae after the acute phase of SARS-CoV-2 infection is relevant for healthcare planning."

Clin Infect Dis: [Population-based estimates of post-acute sequelae of SARS-CoV-2 infection \(PASC\) prevalence and characteristics](#) (19 May 2021)

"Emerging evidence suggests many people have persistent symptoms after acute COVID-19 illness. Our objective was to estimate the prevalence and correlates of post-acute sequelae of SARS-CoV-2 infection (PASC).

We employed a population-based probability survey of adults with COVID-19 in Michigan. Living non-institutionalized adults aged 18+ in the Michigan Disease Surveillance System with COVID-19 onset through mid-April 2020 were eligible for selection ($n=28,000$). Among 2,000 selected, 629 completed the survey between June - December 2020. We estimated PASC prevalence, defined as persistent symptoms 30+ (30-day COVID-19) or 60+ days (60-day COVID-19) post COVID-19 onset, overall and by sociodemographic and clinical factors, including self-reported symptom severity and hospitalization status. We used modified Poisson regression to produce adjusted prevalence ratios (aPR) for potential risk factors.

The analytic sample ($n=593$) was predominantly female (56.1%), aged 45 and older (68.2%), and Non-Hispanic White (46.3%) or Black (34.8%). 30- and 60-day COVID-19 were highly prevalent (52.5% and 35.0%), even among non-hospitalized respondents (43.7% and 26.9%) and respondents reporting mild symptoms (29.2% and 24.5%). Respondents reporting very

severe (vs. mild) symptoms had 2.25 times higher prevalence of 30-day COVID-19 ([aPR] 2.25, 95% CI 1.46-3.46) and 1.71 times higher prevalence of 60-day COVID-19 (aPR 1.71, 95% 1.02-2.88). Hospitalized (vs. non-hospitalized) respondents had about 40% higher prevalence of both 30-day (aPR 1.37, 95% CI 1.12-1.69) and 60-day COVID-19 (aPR 1.40, 95% CI 1.02-1.93).

PASC is highly prevalent among cases reporting severe initial symptoms, and, to a lesser extent, cases reporting mild and moderate symptoms."

JAMA Netw Open: [Global Incidence of Neurological Manifestations Among Patients Hospitalized With COVID-19—A Report for the GCS-NeuroCOVID Consortium and the ENERGY Consortium](#) (11 May 2021)

"Question What are the incidence of and outcomes associated with neurologic manifestations in patients with COVID-19?

Findings In this cohort study of 3744 patients in 2 large consortia, neurological manifestations were found in approximately 80% of patients hospitalized with COVID-19; the most common self-reported symptoms included headache (37%) and anosmia or ageusia (26%), whereas the most common neurological signs and/or syndromes were acute encephalopathy (49%), coma (17%), and stroke (6%). Presence of clinically captured neurologic signs and/or syndromes was associated with increased risk of in-hospital death.

Meaning These findings suggest that neurological manifestations are prevalent among patients hospitalized with COVID-19 and are associated with higher in-hospital mortality."

Mayo Clin Proc: [Post COVID-19 Syndrome \(Long Haul Syndrome\): Description of a Multidisciplinary Clinic at the Mayo Clinic and Characteristics of the Initial Patient Cohort](#) (11 May 2021)

"To describe characteristics of a series of patients reporting prolonged symptoms after an infection with COVID-19.

This study describes the multidisciplinary COVID-19 Activity Rehabilitation Program (CARP), established at Mayo Clinic to evaluate and treat post-COVID-19 syndrome (PCS) patients, and reports the clinical characteristics of the first 100 patients receiving evaluation and management during the timeframe of June 1, 2020 and December 31, 2020.

The cohort consisted of 100 patients (mean age 45 years, 68% women, BMI 30.2, presenting a mean of 93 days after infection). Common pre-existing conditions were respiratory (23%) and mental health, including depression and/or anxiety (34%). The majority (75%) had not been hospitalized for COVID-19. Common presenting symptoms were fatigue (80%), respiratory complaints (59%), and neurologic complaints (59%) followed by subjective cognitive impairment, sleep disturbance, and mental health symptoms. More than one-

third of the patients (34%) reported difficulties with performing basic activities of daily living. Only 1 in 3 patients had returned to unrestricted work duty at the time of the analysis. For most patients, laboratory and imaging studies were normal or non-diagnostic despite debilitating symptoms. Most patients required physical therapy, occupational therapy, or brain rehabilitation. Face-to-face and virtual care delivery modalities were feasible.

Many of the patients did not experience COVID-19-related symptoms that were severe enough to require hospitalization, were younger than 65 years of age, more likely to be female, and most had no pre-existing comorbidities prior to SARS-CoV-2 infection. Symptoms including mood disorders, fatigue, and perceived cognitive impairment resulted in severe negative impacts on resumption of functional and occupational activities in patients experiencing prolonged effects."

Lancet Infect Dis: [Post-acute effects of SARS-CoV-2 infection in individuals not requiring hospital admission: a Danish population-based cohort study](#) (10 May 2021)

"Individuals admitted to hospital for COVID-19 might have persisting symptoms (so-called long COVID) and delayed complications after discharge. However, little is known regarding the risk for those not admitted to hospital. We therefore examined prescription drug and health-care use after SARS-CoV-2 infection not requiring hospital admission.

This was a population-based cohort study using the Danish prescription, patient, and health insurance registries. All individuals with a positive or negative RT-PCR test for SARS-CoV-2 in Denmark between Feb 27 and May 31, 2020, were eligible for inclusion. Outcomes of interest were delayed acute complications, chronic disease, hospital visits due to persisting symptoms, and prescription drug use. We used data from non-hospitalised SARS-CoV-2-positive and matched SARS-CoV-2-negative individuals from 2 weeks to 6 months after a SARS-CoV-2 test to obtain propensity score-weighted risk differences (RDs) and risk ratios (RRs) for initiation of 14 drug groups and 27 hospital diagnoses indicative of potential post-acute effects. We also calculated prior event rate ratio-adjusted rate ratios of overall health-care use. This study is registered in the EU Electronic Register of Post-Authorisation Studies (EUPAS37658).

10 498 eligible individuals tested positive for SARS-CoV-2 in Denmark from Feb 27 to May 31, 2020, of whom 8983 (85.6%) were alive and not admitted to hospital 2 weeks after their positive test. The matched SARS-CoV-2-negative reference population not admitted to hospital consisted of 80 894 individuals. Compared with SARS-CoV-2-negative individuals, SARS-CoV-2-positive individuals were not at an increased risk of initiating new drugs (RD <0.1%) except bronchodilating agents, specifically short-acting β_2 -agonists (117 [1.7%] of 6935 positive individuals vs 743 [1.3%] of 57 206 negative individuals; RD +0.4% [95% CI 0.1–0.7]; RR 1.32 [1.09–1.60]) and triptans (33 [0.4%] of 8292 vs 198 [0.3%] of 72 828; RD

+0.1% [0.0–0.3]; RR 1.55 [1.07–2.25]). There was an increased risk of receiving hospital diagnoses of dyspnoea (103 [1.2%] of 8676 vs 499 [0.7%] of 76 728; RD +0.6% [0.4–0.8]; RR 2.00 [1.62–2.48]) and venous thromboembolism (20 [0.2%] of 8785 vs 110 [0.1%] of 78 872; RD +0.1% [0.0–0.2]; RR 1.77 [1.09–2.86]) for SARS-CoV-2-positive individuals compared with negative individuals, but no increased risk of other diagnoses. Prior event rate ratio-adjusted rate ratios of overall general practitioner visits (1.18 [95% CI 1.15–1.22]) and outpatient hospital visits (1.10 [1.05–1.16]), but not hospital admission, showed increases among SARS-CoV-2-positive individuals compared with SARS-CoV-2-negative individuals.

The absolute risk of severe post-acute complications after SARS-CoV-2 infection not requiring hospital admission is low. However, increases in visits to general practitioners and outpatient hospital visits could indicate COVID-19 sequelae."

See also: [commentary](#)

Diabetes: [New-onset diabetes in "long COVID"](#) (23 April 2021)

Letter to the editor: "Studies published in the Journal of Diabetes and elsewhere demonstrate the increased likelihood of new-onset diabetes (NOD) during the acute phase or shortly after recovering from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing coronavirus disease 2019 (COVID -19).... It is now high time to consider NOD as a metabolic clinical sequela of SARS-CoV-2 infection to understand the role of COVID-19 in driving the diabetes pandemic."

Women's Health, Pregnancy, and Perinatal Care

Peer-Reviewed Articles

JAMA Netw Open: [Trends in Home Birth Information Seeking in the United States and United Kingdom During the COVID-19 Pandemic](#) (17 May 2021)

"This cross-sectional study used online search data to assess changes in home birth information-seeking behaviors across the United States and United Kingdom during the COVID-19 pandemic."

JAMA: [Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women](#) (13 May 2021)

"Question What is the immunogenicity of COVID-19 messenger RNA (mRNA) vaccines in pregnant and lactating women?"

Findings In this cohort study involving 103 women who received a COVID-19 mRNA vaccine, 30 of whom were pregnant and 16 of whom were lactating, immunogenicity was demonstrated in all, and vaccine-elicited antibodies were found in infant cord blood and

breast milk. Pregnant and nonpregnant vaccinated women developed cross-reactive immune responses against SARS-CoV-2 variants of concern.

Meaning In a small convenience sample, COVID-19 mRNA vaccines were immunogenic in pregnant and lactating women and induced immune responses against SARS-CoV-2 variants."

Clin Infect Dis: [Adverse pregnancy outcomes, maternal complications, and severe illness among U.S. delivery hospitalizations with and without a COVID-19 diagnosis](#) (12 May 2021)

"Evidence on risk for adverse outcomes from COVID-19 among pregnant women is still emerging. We examined the association between COVID-19 at delivery and adverse pregnancy outcomes, maternal complications, and severe illness, whether these associations differ by race/ethnicity; and described discharge status by COVID-19 diagnosis and maternal complications.

Data from 703 hospitals in the Premier Healthcare Database during March–September 2020 were included. Adjusted risk ratios overall and stratified by race/ethnicity were estimated using Poisson regression with robust standard errors. Proportion not discharged home was calculated by maternal complications, stratified by COVID-19 diagnosis.

Among 489,471 delivery hospitalizations, 6,550 (1.3%) had a COVID-19 diagnosis. In adjusted models, COVID-19 was associated with increased risk for: acute respiratory distress syndrome (adjusted risk ratio [aRR] = 34.4), death (aRR = 17.0), sepsis (aRR = 13.6), mechanical ventilation (aRR = 12.7), shock (aRR = 5.1), intensive care unit admission (aRR = 3.6), acute renal failure (aRR = 3.5), thromboembolic disease (aRR = 2.7), adverse cardiac event/outcome (aRR = 2.2) and preterm labor with preterm delivery (aRR = 1.2). Risk for any maternal complications or for any severe illness did not significantly differ by race/ethnicity. Discharge status did not differ by COVID-19; however, among women with concurrent maternal complications, a greater proportion of those with (versus without) COVID-19 were not discharged home.

These findings emphasize the importance of implementing recommended mitigation strategies to reduce risk for SARS-CoV-2 infection and further inform counseling and clinical care for pregnant women during the COVID-19 pandemic."

JAMA Netw Open: [Perinatal Outcomes During the COVID-19 Pandemic in Ontario, Canada](#) (12 May 2021)

"This cohort study evaluates rates of preterm birth and stillbirth in Ontario, Canada, during the first 6 months of the COVID-19 pandemic."

Ann Intern Med: [In-Hospital Mortality in a Cohort of Hospitalized Pregnant and Nonpregnant Patients With COVID-19](#) (11 May 2021)

"To evaluate the risk for in-hospital death among pregnant and nonpregnant patients of reproductive age hospitalized with COVID-19, because studies with more thorough ascertainment of COVID-19 in pregnancy are needed to provide the foundation for clinical management and health care policy....

In this large, geographically diverse cohort of reproductive-aged patients hospitalized with COVID-19, we found that in-hospital mortality was low in pregnant patients."

Front Psychol: [Communication Across Maternal Social Networks During England's First National Lockdown and Its Association With Postnatal Depressive Symptoms](#) (11 May 2021)

"Postnatal/postpartum depression (PND/PPD) had a pre-COVID-19 estimated prevalence ranging up to 23% in Europe, 33% in Australia, and 64% in America, and is detrimental to both mothers and their infants. Low social support is a key risk factor for developing PND. From an evolutionary perspective this is perhaps unsurprising, as humans evolved as cooperative childrears, inherently reliant on social support to raise children. The coronavirus pandemic has created a situation in which support from social networks beyond the nuclear family is likely to be even more important to new mothers, as it poses risks and stresses for mothers to contend with; whilst at the same time, social distancing measures designed to limit transmission create unprecedented alterations to their access to such support. Using data from 162 mothers living in London with infants aged ≤ 6 months, we explore how communication with members of a mother's social network related to her experience of postnatal depressive symptoms during the first "lockdown" in England. Levels of depressive symptoms, as assessed via the Edinburgh Postnatal Depression Scale, were high, with 47.5% of the participants meeting a ≥ 11 cut-off for PND. Quasi-Poisson regression modelling found that the number of network members seen in-person, and remote communication with a higher proportion of those not seen, was negatively associated with depressive symptoms; however, contact with a higher proportion of relatives was positively associated with symptoms, suggesting kin risked seeing mothers in need. Thematic qualitative analysis of open text responses found that mothers experienced a burden of constant mothering, inadequacy of virtual contact, and sadness and worries about lost social opportunities, while support from partners facilitated family bonding. While Western childrearing norms focus on intensive parenting, and fathers are key caregivers, our results highlight that it still "takes a village" to raise children in high-income populations and mothers are struggling in its absence."

J Clin Invest: [Severe SARS-CoV-2 placenta infection can impact neonatal outcome in the absence of vertical transmission](#) (15 March 2021)

"The effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on the pathophysiology of the placenta and its impact on pregnancy outcome has not yet been fully elucidated. Here, we present a comprehensive clinical, morphological, and molecular

analysis of placental tissues from pregnant women with and without SARS-CoV-2 infection. SARS-CoV-2 could be detected in half of placental tissues from SARS-CoV-2–positive women. The presence of the virus was not associated with any distinctive pathological, maternal, or neonatal outcome features. SARS-CoV-2 tissue load was low in all but one patient who exhibited severe placental damage leading to neonatal neurological manifestations. The placental transcriptional response induced by high viral load of SARS-CoV-2 showed an immunopathology phenotype similar to autopsy lung tissues from patients with severe coronavirus disease 2019. This finding contrasted with the lack of inflammatory response in placental tissues from SARS-CoV-2–positive women with low viral tissue load and from SARS-CoV-2–negative women. Importantly, no evidence of vertical transmission of SARS-CoV-2 was found in any newborns, suggesting that the placenta may be an effective maternal-neonatal barrier against the virus even in the presence of severe infection. Our observations suggest that severe placental damage induced by the virus may be detrimental for the neonate independently of vertical transmission."

Pediatric Population

Peer-Reviewed Articles

MMWR: [Mask Use and Ventilation Improvements to Reduce COVID-19 Incidence in Elementary Schools — Georgia, November 16–December 11, 2020](#) (21 May 2021)

"What is already known about this topic? Kindergarten through grade 5 schools educate and address the students' physical, social, and emotional needs. Preventing SARS-CoV-2 transmission in schools is imperative for safe in-person learning.

What is added by this report? COVID-19 incidence was 37% lower in schools that required teachers and staff members to use masks and 39% lower in schools that improved ventilation. Ventilation strategies associated with lower school incidence included dilution methods alone (35% lower incidence) or in combination with filtration methods (48% lower incidence).

What are the implications for public health practice? Mask requirements for teachers and staff members and improved ventilation are important strategies in addition to vaccination of teachers and staff members that elementary schools could implement as part of a multicomponent approach to provide safer, in-person learning environments."

JAMA Netw Open: [Assessment of Feasibility of Face Covering in School-Aged Children With Autism Spectrum Disorders and Attention-Deficit/Hyperactivity Disorder](#) (17 May 2021)

"This cohort study reports the outcomes of using positive behavior supports to promote masking in school-aged children with autism spectrum disorders (ASD) and/or attention-deficit/hyperactivity disorder (ADHD) attending a summer day treatment program."

MMWR: [The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine in Adolescents Aged 12–15 Years — United States, May 2021](#) (14 May 2021)

"What is already known about this topic? On May 10, 2021, the Food and Drug Administration expanded Emergency Use Authorization for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years.

What is added by this report? On May 12, 2021, after a systematic review of all available data, the Advisory Committee on Immunization Practices made an interim recommendation for use of the Pfizer-BioNTech COVID-19 vaccine in adolescents aged 12–15 years for the prevention of COVID-19.

What are the implications for public health practice? The Pfizer-BioNTech COVID-19 vaccine is the first COVID-19 vaccine approved for use in adolescents and has high efficacy against symptomatic COVID-19. Vaccination will be important to protect adolescents against symptomatic COVID-19 disease and to reduce community transmission of SARS-CoV-2."

Arch Dis Child Fetal Neonatal Ed: [Coronavirus infection in neonates: a systematic review](#) (20 April 2021)

"Objective To summarise currently reported neonatal cases of SARS-CoV-2 infection.

Methods A search strategy was designed to retrieve all articles published from 1 December 2019 to 12 May 2020, by combining the terms 'coronavirus' OR 'covid' OR 'SARS-CoV-2') AND ('neonat*' OR 'newborn') in the following electronic databases: MEDLINE/Pubmed, Scopus, Web of Science, MedRxiv, the Cochrane Database of Systematic Review and the WHO COVID-19 database, with no language restrictions. Quality of studies was evaluated by using a specific tool for assessment of case reports and/or case series.

Results Twenty-six observational studies (18 case reports and 8 case series) with 44 newborns with confirmed SARS-CoV-2 infection were included in the final analysis. Studies were mainly from China and Italy. Half of neonates had a documented contact with the infected mother and one out of three infected neonates was admitted from home. Median age at diagnosis was 5 days. One out of four neonates was asymptomatic, and the remaining showed mild symptoms typical of acute respiratory infections and/or gastrointestinal symptoms. The majority of neonates were left in spontaneous breathing (room air) and had good prognosis after a median duration of hospitalisation of 10 days.

Conclusions Most neonates with SARS-CoV-2 infection were asymptomatic or presented mild symptoms, generally were left in spontaneous breathing and had a good prognosis after median 10 days of hospitalisation. Large epidemiological and clinical cohort studies, as well as the implementation of collaborative networks, are needed to improve the understanding of the impact of SARS-CoV-2 infection in neonates."

Disparities and Health Equity

News in Brief

"Stark racial disparities persist in vaccinations, state-level CDC data shows" ([KHN](#)).

"Latinos are the most eager to get vaccinated, survey shows — but face obstacles" ([KHN](#)).

"Vaccinating children before poor morally wrong, Oxford scientist says" ([BBC](#); see also: "American kids can wait" from [The Atlantic](#)).

"Hospitals serving the poor struggled during COVID. Wealthy hospitals made millions" ([NPR](#)).

Peer-Reviewed Articles

JAMA Netw Open: [Community Factors Associated With Telemedicine Use During the COVID-19 Pandemic](#) (18 May 2021)

"This cross-sectional study investigates which community factors may be associated with the increase in telemedicine use during the COVID-19 pandemic."

MMWR: [Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties — United States, December 14, 2020–April 10, 2021](#) (18 May 2021)

"What is already known about this topic? Residents of rural communities are at increased risk for severe COVID-19–associated morbidity and mortality. In September 2020, COVID-19 incidence (cases per 100,000 population) in rural counties surpassed that in urban counties.

What is added by this report? COVID-19 vaccination coverage was lower in rural counties (38.9%) than in urban counties (45.7%); disparities persisted among age groups and by sex.

What are the implications for public health practice? Disparities in COVID-19 vaccination access and coverage between urban and rural communities can hinder progress toward ending the pandemic. Public health practitioners should collaborate with health care providers, pharmacies, employers, faith leaders, and other community partners to identify and address barriers to COVID-19 vaccination in rural areas."

Nat Med: [Equitable allocation of COVID-19 vaccines in the United States](#) (18 May 2021)

"Many vaccine rationing guidelines urge planners to recognize, and ideally reduce, inequities. In the United States, allocation frameworks are determined by each of the Centers for Disease Control and Prevention's 64 jurisdictions (50 states, the District of Columbia, five cities and eight territories). In this study, we analyzed vaccine allocation plans published by 8 November 2020, tracking updates through to 30 March 2021. We evaluated whether jurisdictions adopted proposals to reduce inequity using disadvantage indices and related place-based measures.

By 30 March 2021, 14 jurisdictions had prioritized specific zip codes in combination with metrics such as COVID-19 incidence, and 37 jurisdictions (including 34 states) had adopted disadvantage indices, compared to 19 jurisdictions in November 2020. Uptake of indices doubled from 7 to 14 among the jurisdictions with the largest shares of disadvantaged communities.

Five applications were distinguished: (1) prioritizing disadvantaged groups through increased shares of vaccines or vaccination appointments; (2) defining priority groups or areas; (3) tailoring outreach and communication; (4) planning the location of dispensing sites; and (5) monitoring receipt. To ensure that equity features centrally in allocation plans, policymakers at the federal, state and local levels should universalize the uptake of disadvantage indices and related place-based measures."

Risk, Transmission, Exposure, and Testing

News in Brief

"Basically everyone is mad at the CDC for being so confusing about masks" ([BuzzFeed](#)).

Once facing severe shortages with high demand, now we have massive surplus of masks following the CDC's new guidelines ([CBS](#)).

"The myriad ways sewage surveillance is helping fight COVID around the world: Wastewater tracking was used before the pandemic to monitor for polio and illicit drug use, but interest in the field and its applications has now ballooned" ([Nature](#)).

Long read: "The 60-year-old scientific screwup that helped Covid kill: All pandemic long, scientists brawled over how the virus spreads. Droplets! No, aerosols! At the heart of the fight was a teensy error with huge consequences" ([Wired](#); requires free signup to read).

Peer-Reviewed Articles

Emerg Infect Dis: [SARS-CoV-2 Superspread in Fitness Center, Hong Kong, China, March 2021](#) (18 May 2021)

"To investigate a superspreading event at a fitness center in Hong Kong, China, we used genomic sequencing to analyze 102 reverse transcription PCR–confirmed cases of severe acute respiratory syndrome coronavirus 2 infection. Our finding highlights the risk for virus transmission in confined spaces with poor ventilation and limited public health interventions."

Nat Commun: [A rapid, accurate, scalable, and portable testing system for COVID-19 diagnosis](#) (18 May 2021)

"The need for rapid, accurate, and scalable testing systems for COVID-19 diagnosis is clear and urgent. Here, we report a rapid Scalable and Portable Testing (SPOT) system consisting of a rapid, highly sensitive, and accurate assay and a battery-powered portable device for COVID-19 diagnosis. The SPOT assay comprises a one-pot reverse transcriptase-loop-mediated isothermal amplification (RT-LAMP) followed by PfAgo-based target sequence detection. It is capable of detecting the N gene and E gene in a multiplexed reaction with the limit of detection (LoD) of 0.44 copies/μL and 1.09 copies/μL, respectively, in SARS-CoV-2 virus-spiked saliva samples within 30 min. Moreover, the SPOT system is used to analyze 104 clinical saliva samples and identified 28/30 (93.3% sensitivity) SARS-CoV-2 positive samples (100% sensitivity if LoD is considered) and 73/74 (98.6% specificity) SARS-CoV-2 negative samples. This combination of speed, accuracy, sensitivity, and portability will enable high-volume, low-cost access to areas in need of urgent COVID-19 testing capabilities."

J Infect Dis: [Comparable environmental stability and disinfection profiles of the currently circulating SARS-CoV-2 variants of concern B.1.1.7 and B.1.351](#) (16 May 2021)

"The emergence of novel SARS-CoV-2 B.1.1.7 and B.1.351 variants of concern with increased transmission dynamics has raised questions regarding stability and disinfection of these viruses. In this study, we analyzed surface stability and disinfection of the currently circulating SARS-CoV-2 variants B.1.1.7 and B.1.351 compared to the wild type. Treatment with heat, soap and ethanol revealed similar inactivation profiles indicative of a comparable susceptibility towards disinfection. Furthermore, we observed comparable surface stability on steel, silver, copper and face masks. Overall, our data support the application of currently recommended hygiene concepts to minimize the risk of B.1.1.7 and B.1.351 transmission."

Clin Infect Dis: [Cruise ship travel in the era of COVID-19: A summary of outbreaks and a model of public health interventions](#) (12 May 2021)

"Cruise travel contributed to SARS-CoV-2 transmission when there were relatively few cases in the United States. By March 14, 2020, the Centers for Disease Control and Prevention (CDC) issued a No Sail Order suspending U.S. cruise operations; the last U.S. passenger ship docked on April 16.

We analyzed SARS-CoV-2 outbreaks on cruises in U.S. waters or carrying U.S. citizens and used regression models to compare voyage characteristics. We used compartmental models to simulate the potential impact of four interventions (screening for COVID-19 symptoms; viral testing on two days and isolation of positive persons; reduction of passengers by 40%, crew by 20%, and port visits to one) for 7-day and 14-day voyages.

During January 19–April 16, 2020, 89 voyages on 70 ships had known SARS-CoV-2 outbreaks; 16 ships had recurrent outbreaks. There were 1,669 RT-PCR-confirmed SARS-CoV-2 infections and 29 confirmed deaths. Longer voyages were associated with more cases (adjusted incidence rate ratio, 1.10, 95% CI: 1.03-1.17, $p < 0.0001$). Mathematical models showed that 7-day voyages had about 70% fewer cases than 14-day voyages. On 7-day voyages, the most effective interventions were reducing the number of individuals onboard (43-49% reduction in total infections) and testing passengers and crew (42-43% reduction in total infections). All four interventions reduced transmission by 80%, but no single intervention or combination eliminated transmission. Results were similar for 14-day voyages.

SARS-CoV-2 outbreaks on cruises were common during January-April 2020. Despite all interventions modeled, cruise travel still poses a significant SARS-CoV-2 transmission risk."

Prehosp Emerg Care: [SARS-CoV-2 IgG Seropositivity and Acute Asymptomatic Infection Rate among Firefighter First Responders in an Early Outbreak County in California](#) (06 May 2021)

"Objective: Firefighter first responders and other emergency medical services (EMS) personnel have been among the highest risk healthcare workers for illness during the SARS-CoV-2 pandemic. We sought to determine the rate of seropositivity for SARS-CoV-2 IgG antibodies and of acute asymptomatic infection among firefighter first responders in a single county with early exposure in the pandemic.

Methods: We conducted a cross-sectional study of clinically active firefighters cross-trained as paramedics or EMTs in the fire departments of Santa Clara County, California. Firefighters without current symptoms were tested between June and August 2020. Our primary outcomes were rates of SARS-CoV-2 IgG antibody seropositivity and SARS-CoV-2 RT-PCR swab positivity for acute infection. We report cumulative incidence, participant characteristics with frequencies and proportions, and proportion positive and associated relative risk (with 95% confidence intervals).

Results: We enrolled 983 out of 1339 eligible participants (response rate: 73.4%). Twenty-five participants (2.54%, 95% CI 1.65-3.73) tested positive for IgG antibodies and 9 (0.92%, 95% CI 0.42-1.73) tested positive for SARS-CoV-2 by RT-PCR. Our cumulative incidence, inclusive of self-reported prior positive PCR tests, was 34 (3.46%, 95% CI 2.41-4.80).

Conclusion: In a county with one of the earliest outbreaks in the United States, the seroprevalence among firefighter first responders was lower than that reported by other studies of frontline health care workers, while the cumulative incidence remained higher than that seen in the surrounding community."

PNAS: [A guideline to limit indoor airborne transmission of COVID-19](#) (27 April 2021)

"The current revival of the American economy is being predicated on social distancing, specifically the Six-Foot Rule, a guideline that offers little protection from pathogen-bearing aerosol droplets sufficiently small to be continuously mixed through an indoor space. The importance of airborne transmission of COVID-19 is now widely recognized. While tools for risk assessment have recently been developed, no safety guideline has been proposed to protect against it. We here build on models of airborne disease transmission in order to derive an indoor safety guideline that would impose an upper bound on the "cumulative exposure time," the product of the number of occupants and their time in an enclosed space. We demonstrate how this bound depends on the rates of ventilation and air filtration, dimensions of the room, breathing rate, respiratory activity and face mask use of its occupants, and infectiousness of the respiratory aerosols. By synthesizing available data from the best-characterized indoor spreading events with respiratory drop size distributions, we estimate an infectious dose on the order of 10 aerosol-borne virions. The new virus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) is thus inferred to be an order of magnitude more infectious than its forerunner (SARS-CoV), consistent with the pandemic status achieved by COVID-19. Case studies are presented for classrooms and nursing homes, and a spreadsheet and online app are provided to facilitate use of our guideline. Implications for contact tracing and quarantining are considered, and appropriate caveats enumerated. Particular consideration is given to respiratory jets, which may substantially elevate risk when face masks are not worn."

J Sports Med Phys Fitness: [COVID-19 and physical activity in sedentary individuals: differences in metabolic, cardiovascular, and respiratory responses during aerobic exercise performed with and without a surgical face masks](#) (22 April 2021)

"BACKGROUND: The Coronavirus-19 (COVID-19) impairs metabolic, cardiovascular, and pulmonary functions in human metabolism, and wearing face masks is recommended for the prevention of contracting or exposing others to cardio-respiratory infections. Since the effect of wearing a surgical face mask (SFM) on cardiopulmonary exercise capacity has not been systematically reported we aimed to determine the effects of wearing SFM during an

incremental walking test on metabolic, cardiovascular, and pulmonary gas exchange responses in sedentary individuals.

METHODS: The evaluations were performed using a repeated measures study design. Seven sedentary males (age:40years, height:178cm, weight:88kg, BMI:28kg/m², VO₂max:32.7±3.9ml/kg/min) and 7 sedentary female participants (age:34years, height:169cm, weight:62kg, BMI:22kg/m², VO₂max:32.1±6.8 ml/kg/min) volunteered to participate in the current study. Anthropometric parameters were measured using a Bioelectrical impedance analysis prior to each testing session. The measures of lung function assessed by spirometry, breathing pattern, maximal exercise capacity with-and-without mask were measured with a breath-by-breath automated exercise metabolic system during incremental Bruce protocol on a treadmill with two consecutive sessions with 48-h intervals. Blood pressure values (systolic and diastolic pressure) of the individuals were taken and recorded within 1 minute at the end of every ten minutes, without speed changes.

RESULTS: VO₂, VCO₂, and VE were significantly lower during exercise performed with SFM (p<0.001). Heart rate, systolic and diastolic blood pressure were also found significantly higher during exercise performed with SFM (p<0.01).

CONCLUSIONS: Wearing a SFM during incremental walking predispose a decrease in oxygen delivery while increasing pulmonary ventilation in sedentary individuals. Thus, it could be speculated that surgical face masks have a negative impact on oxygen delivery during exercise which results in decreased exercise performance due to the restricted ventilatory conditions."

Impact on Healthcare Workers

Special Reports and Other Resources

Medscape: [The Doctor's Dilemma of Overcoming Burnout](#)

This series of videos (also available as podcasts) on physician burnout includes CME activities.

"Healthcare workers are experiencing tremendous stress and fatigue. Burnout is occurring in significant numbers among doctors and nurses, with half by some reports exhibiting symptoms, even before the COVID-19 pandemic. This mini series aims to discuss this with experts and those who have experienced it, and showcase innovative solutions to help with burnout and promote resiliency. Join Dr Hansa Bhargava and her guests for the next several weeks to learn more."

NAM: [Clinicians and Professional Societies COVID-19 Impact Assessment: Lessons Learned and Compelling Needs](#) (17 May 2021)

Discussion paper that touches on the factors impacting clinician response to COVID-19. Includes comments on key challenges such as: burnout; staffing and operations; disparities in health, finances, and educational (GME and other) access; and policy considerations.

This paper is part of a larger series from the National Academy of Medicine: "Emerging Stronger After COVID-19: Priorities for Health System Transformation"; for more reports and forthcoming topics, see: <https://nam.edu/programs/value-science-driven-health-care/emerging-stronger-after-covid-19-priorities-for-health-system-transformation/>

Reinfections, Coinfection, and Other Infectious Diseases

News in Brief

"Mucormycosis: The 'black fungus' maiming Covid patients in India" ([BBC](#)).

"After year with virtually no flu, scientists worry the next season could be a bad one – a nearly nonexistent flu season means normally high levels of immunity are much lower" ([NBC](#)).

"The overlooked, dangerous nexus between national security and public health: the case of smallpox. One of public health's greatest triumphs arguably led to major gaps in health and national security" ([GSR](#)).

Mystery Diseases

"US investigates second suspected case of mystery 'syndrome' near White House" ([CNN](#)).

A different mystery illness: "A mysterious, devastating brain disorder is afflicting dozens in one Canadian province" ([WP](#); see also: [New Brunswick Public Health](#)).

Other Outbreaks

Chronic wasting disease has been detected in a deer from Virginia's Montgomery County ([VA DWR](#)).

"Health Officials in Kween District in Eastern Uganda are reporting 15 people are undergoing treatment for anthrax and over 15 heads of cattle have so far succumbed to the disease since last month" ([ONT](#)).

"Johnson & Johnson offer up to 200,000 vaccine regimens for WHO use on Ebola in Sierra Leone" ([HPN](#)).

Webinars

- WHEN: Wednesday, 26 May 2021, 100-1200 ET
- WHAT: U.S. Leadership for a Pandemic-Free Future: Technologies to End Biological Threats – The Capitol Hill Steering Committee on Pandemic Preparedness & Health Security
- DETAILS: "This webinar will explore how the federal government can prioritize investments in available and future technologies to ensure nothing like the Covid-19 pandemic, or worse, could ever happen again."
- REGISTER: https://jh.zoom.us/webinar/register/WN_bE6b6oFDSyS3C2a3WWEleA

Peer-Reviewed Articles

Clin Infect Dis: [Risk of SARS-CoV-2 reinfection in a university student population](#) (16 May 2021)

"We assess protection from previous SARS-CoV-2 infection in a population of 16,101 university students (2,021 with and 14,080 without previous infection). The risk of re-infection during the Spring 2021 semester was 2.2% among previously infected students; estimated protection from previous SARS-CoV-2 infection was 84% (95% CI: 78%-88%)."

MMWR: [Surveillance of Vaccination Coverage Among Adult Populations — United States, 2018](#) (14 May 2021)

"NHIS [National Health Interview Survey] data indicate that many adults remain unprotected against vaccine-preventable diseases. Coverage for the adult age-appropriate composite measures was low in all age groups. Individual adult vaccination coverage remained low as well, but modest gains occurred in vaccination coverage for hepatitis B (among adults aged ≥19 years and HCP aged ≥19 years), and HPV (among males aged 19–26 years and Hispanic females aged 19–26 years). Coverage for other vaccines and groups with Advisory Committee on Immunization Practices vaccination indications did not improve from 2017. Although HPV vaccination coverage among males aged 19–26 years and Hispanic females aged 19–26 years increased, approximately 50% of females aged 19–26 years and 70% of males aged 19–26 years remained unvaccinated. Racial/ethnic vaccination differences persisted for routinely recommended adult vaccines. Having health insurance coverage, having a usual place for health care, and having ≥1 physician contacts during the preceding 12 months were associated with higher vaccination coverage; however, these factors alone were not associated with optimal adult vaccination coverage, and findings indicate missed opportunities to vaccinate remained."

Emerg Infect Dis: [Case Series of Laboratory-Associated Zika Virus Disease, United States, 2016–2019](#) (published online 14 April 2021; May 2021 issue)

"Zika virus diagnostic testing and laboratory research increased considerably when Zika virus began spreading through the Americas in 2015, increasing the risk for potential Zika virus exposure of laboratory workers and biomedical researchers. We report 4 cases of laboratory-associated Zika virus disease in the United States during 2016–2019. Of these, 2 were associated with needlestick injuries; for the other 2 cases, the route of transmission was undetermined. In laboratories in which work with Zika virus is performed, good laboratory biosafety practices must be implemented and practiced to reduce the risk for infection among laboratory personnel."

PLoS One: [Inappropriate antibiotic use in the COVID-19 era: Factors associated with inappropriate prescribing and secondary complications. Analysis of the registry SEMI-COVID](#) (11 May 2021)

"The SEMI-COVID-19 Registry is a multicenter, retrospective patient cohort. Patients with antibiotic were divided into two groups according to appropriate or inappropriate prescription, depending on whether the patient fulfill any criteria for its use. Comparison was made by means of multilevel logistic regression analysis. Possible complications of antibiotic use were also identified.

Out of 13,932 patients, 3047 (21.6%) were prescribed no antibiotics, 6116 (43.9%) were appropriately prescribed antibiotics, and 4769 (34.2%) were inappropriately prescribed antibiotics. The following were independent factors of inappropriate prescription: February–March 2020 admission (OR 1.54, 95%CI 1.18–2.00), age (OR 0.98, 95%CI 0.97–0.99), absence of comorbidity (OR 1.43, 95%CI 1.05–1.94), dry cough (OR 2.51, 95%CI 1.94–3.26), fever (OR 1.33, 95%CI 1.13–1.56), dyspnea (OR 1.31, 95%CI 1.04–1.69), flu-like symptoms (OR 2.70, 95%CI 1.75–4.17), and elevated C-reactive protein levels (OR 1.01 for each mg/L increase, 95% CI 1.00–1.01). Adverse drug reactions were more frequent in patients who received ANTIBIOTIC (4.9% vs 2.7%, $p < .001$).

The inappropriate use of antibiotics was very frequent in COVID-19 patients and entailed an increased risk of adverse reactions. It is crucial to define criteria for their use in these patients. Knowledge of the factors associated with inappropriate prescribing can be helpful."

Clin Infect Dis: [Interacting Epidemics in Amazonian Brazil: Prior Dengue Infection Associated with Increased COVID-19 Risk in a Population-Based Cohort Study](#) (06 May 2021)

"Immunity after dengue virus (DENV) infection has been suggested to cross-protect from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and mortality.

We tested whether serologically proven prior DENV infection diagnosed in September-October 2019, before the coronavirus 2019 (COVID-19) pandemic, reduced the risk of SARS-CoV-2 infection and clinically apparent COVID-19 over the next 13 months in a population-based cohort in Amazonian Brazil. Mixed-effects multiple logistic regression analysis was used to identify predictors of infection and disease, adjusting for potential individual and household-level confounders. Virus genomes from 14 local SARS-CoV-2 isolates were obtained using whole-genome sequencing.

Anti-DENV IgG was found in 37.0% of 1,285 cohort participants (95% confidence interval [CI], 34.3% to 39.7%) in 2019, with 10.4 (95% CI, 6.7 to 15.5) seroconversion events per 100 person-years during the follow-up. In 2020, 35.2% of the participants (95% CI, 32.6% to 37.8%) had anti-SARS-CoV-2 IgG and 57.1% of the 448 SARS-CoV-2 seropositives (95% CI, 52.4% to 61.8%) reported clinical manifestations at the time of infection. Participants aged >60 y were twice more likely to have symptomatic COVID-19 than under-five children. Locally circulating SARS-CoV-2 isolates were assigned to the B.1.1.33 lineage. Contrary to the cross-protection hypothesis, prior DENV infection was associated with twice the risk of clinically apparent COVID-19 upon SARS-CoV-2 infection, with P values between 0.025 and 0.039 after adjustment for identified confounders.

Higher risk of clinically apparent COVID-19 among individuals with prior dengue has important public health implications for communities sequentially exposed to DENV and SARS-CoV-2 epidemics."

Statistics

Global

21 MAY 2021: 165,622,040 confirmed cases and 3,432,517 deaths

United States

top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	33,057,486	3,774,378	2,938,307	2,302,489	2,091,342	1,371,791
Deaths	588,548	62,817	51,128	36,347	53,070	24,913

[JHU CSSE](#) as of 1000 EDT 21 May 2021

Virginia

	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	677,312	20,989	10,506	14,036	17,770	9,084	7,948	36,025
Hospitalizations	29,441	1,002	386	456	1,003	676	452	1,638
Deaths	11,074	298	178	228	259	197	191	403

[VA DOH](#) as of 1000 EDT 21 May 2021